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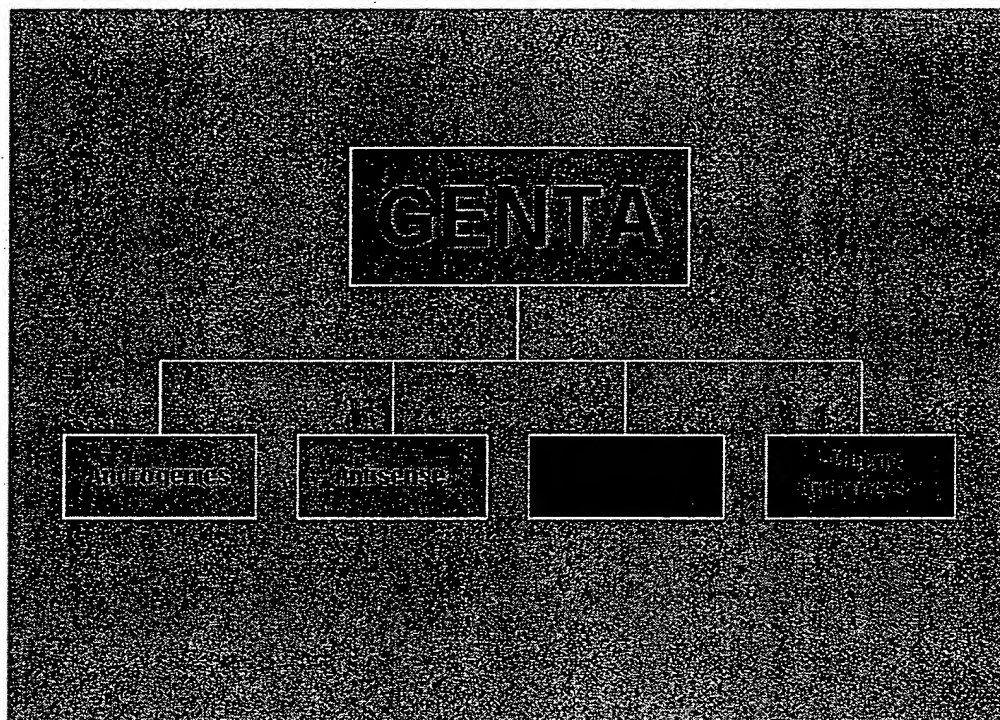
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## Company Profile



Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on anticancer therapy. Genta's research program is anchored by 4 key components: **Antisense Technology**; **Androgenics Products**; **Gallium Products**; and **Decoy Aptamers**. The products from each of these platforms address significant unmet medical needs. The market potential of each program individually exceeds \$1 billion dollars in annual revenues.

The Company's lead antisense compound, Genasense™, is currently in late-stage clinical trials for treatment of melanoma, multiple myeloma and chronic lymphocytic leukemia. Other current studies with Genasense™ target acute myeloid leukemia and cancers of the prostate, lung, colon, and breast. Genasense™ is being used to enhance the activity of other standard types of anticancer therapy. The drug has received both "Fast Track" and "Orphan Drug" designation from the U.S. Food and Drug Administration.

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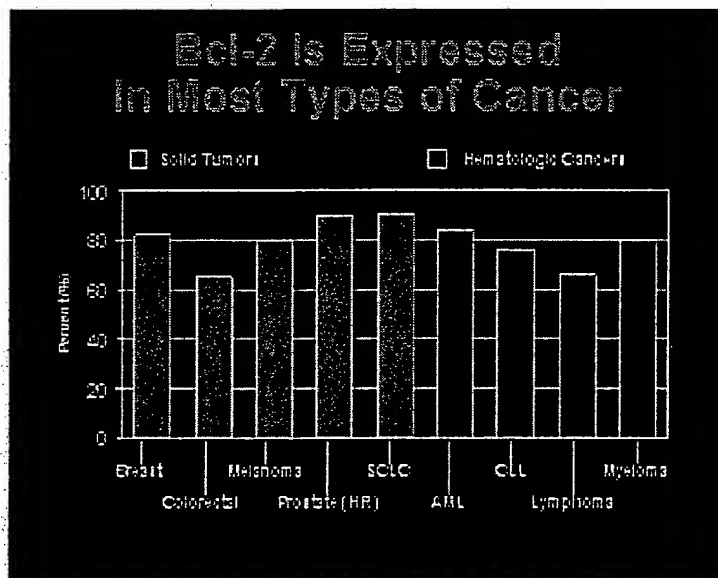
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## Genasense™

Genasense™ is an antisense drug that blocks the production of *Bcl-2*. By reducing production of *Bcl-2* in cancer cells, Genasense™ treatment biological process whereby cancer cells can be readily killed by treatment with current methods of anticancer therapy. There are several key features of Genta's approach to cancer treatment with Genasense™.

### Bcl-2 is Widely Expressed in Many Types of Cancer

As shown in the diagram below, *Bcl-2* – the protein targeted by Genasense™ – is broadly expressed in most common types of cancer. Genta is planning clinical trials in a number of these illnesses, including melanoma, myeloma, acute myeloid leukemia, chronic lymphocytic leukemia, and prostate cancer.



### Genasense™ Synergizes with Most Types of Anticancer Therapy

Preliminary studies have shown that Genasense™ synergizes with almost all types of anticancer treatment, including chemotherapy, radiation, and surgery. Based on preliminary data, Genta has conducted preliminary clinical trials using Genasense™ in combination with:

- Paclitaxel (Taxol®; Bristol Myers Squibb)
- Docetaxel (Taxotere®; Aventis Pharmaceuticals)
- Irinotecan (Camptosar®; Pharmacia, Inc.)
- Gemtuzumab ozogamicin (Mylotarg®; Wyeth-A Inc.)
- Fludarabine (Fludara®; Berlex Laboratories, Inc.)
- Cytosine arabinoside
- Cyclophosphamide (Cytoxan®; Bristol Myers Squibb, Inc.)
- Dexamethasone

### Genasense™ Development Strategy

Genta is using Genasense™ to potentiate the cancer-killing activity of standard anticancer therapy. The side-effects of Genasense™ do not add to the side-effects of current methods of cancer treatment. Thus, alteration in either the dose or schedule of such therapy is usually not required for a physician to use Genasense™. In a typical example, Genasense™ might be used as a pre-treatment for several days, which would then be immediately followed by regular doses of chemotherapy. The sequence would then be repeated, depending upon the particular type of chemotherapy program.

It is a key feature of Genta's development strategy that Genasense™ enhances - and does not compete with - other forms of anticancer therapy. The goal is to be used to "Optimize the State-of-the-Art of Cancer Treatment".

### The Genasense™ Opportunity

The potential for Genasense™ can be reduced to the equation below:

High Bcl-2 Expression in Many Types of  
Cancer

+

Broad Synergy with Many Types of Anticancer Treatment

By comparison, Genta is the only company with:



A fully validated antisense attack on its target



A target that is highly expressed in a markedly larger number of cancer types



A target that has no current competition in the clinic



An antisense drug that is in Phase 3 testing in several different cancer types

## **Clinical Trials**

### **Phase 3 Trial in Chronic Lymphocytic Leukemia**

This randomized trial tests whether the addition of Genasense to standard treatment is superior to standard treatment alone. Standard treatment is cyclical treatment with a combination of two chemotherapy drugs, fludarabine and cyclophosphamide. The trial is limited to patients who have previously received and have relapsed from other therapies.

### **Phase 3 Trial in Malignant Melanoma**

This randomized trial tests whether the addition of Genasense to standard treatment is superior to standard treatment alone. Standard treatment is drug called dacarbazine (DTIC), which is administered once every 3 weeks. This trial is limited to patients with advanced-stage disease who have previously received chemotherapy. (Prior vaccine or immunotherapy is allowed.)

### **Phase 3 Trial in Multiple Myeloma**

This randomized trial tests whether the addition of Genasense to standard treatment is superior to standard treatment alone. Standard treatment is cyclical treatment with high-dose dexamethasone (a corticosteroid-like drug). The trial is limited to patients who have previously received and have relapsed from other therapies.

### **Randomized Trial in Non-Small Cell Lung Cancer**

This randomized trial tests whether the addition of Genasense to a standard treatment is superior to standard treatment alone. Standard treatment is docetaxel (a taxane), which is administered once every 3 weeks. This trial is limited to patients with advanced disease who have been with one prior chemotherapy regimen.

### **Phase 2 Trial in Acute Myeloid Leukemia**

This non-randomized trial tests whether the addition of Genasense to a newly approved standard treatment is superior to recent experience with standard care alone. The accompanying drug in this trial is Mylotarg® (gemtuzumab ozogamicin), a monoclonal antibody conjugated with doxorubicin. This trial is limited to patients over the age of 60 who have relapsed from standard first-line chemotherapy.

### **Phase 2 Trial in Chronic Lymphocytic Leukemia**

This non-randomized trial evaluates the safety and efficacy of Genasense as a single agent in patients with CLL. The trial is limited to patients who have previously received fludarabine in at least one of their prior therapies.

### **Phase 2 Trial in Mantle Cell Lymphoma**

This non-randomized trial tests the single agent safety and activity of Genasense in patients with Mantle Cell Lymphoma. In addition, it will test the safety and activity of Genasense in combination with R-CHOP (a combination of a monoclonal antibody with chemotherapy) for patients who do not receive treatment with Genasense alone.

### **Phase 2 Trial in Prostate**

This non-randomized trial tests whether the addition of Genasense to a standard treatment is superior to recent experience using the standard treatment alone. The standard drug in this trial is docetaxel (a taxane), which is administered once every 3 weeks. This trial is limited to hormone-naïve patients.

All of the Company's clinical trials have additional restrictions and provisions for safety that may affect patient eligibility. Physicians who wish to refer patients for consideration regarding entry into the trials, or who require information regarding current participating sites should contact the Company by e-mail at: [ClinicalTrials@genta.com](mailto:ClinicalTrials@genta.com); or by telephone at: 908-286-9800. Clinical trial sites are subject to change during the course of clinical trials.

## Overview of the Genasense™ Clinical Program

Preliminary clinical studies of Genasense™ have reported activity for Genasense™ used alone. However, the drug is primarily being investigated to potentiate standard forms of cancer treatment. Laboratory studies clearly suggest that Genasense™ can markedly increase the effectiveness of standard forms of cancer treatment and the current clinical program is set up to carefully test that idea.

Given the contribution of *Bcl-2* expression to chemotherapy resistance, the Company's programs are testing the use of Genasense™ as a pre-treatment to reduce *Bcl-2* protein levels as low as possible, and then to administer state-of-the-art cancer therapy. Our Phase 3 studies are designed to test whether this combined approach will be associated with significant benefit to patients.

Randomized Phase 3 clinical trials of Genasense™ sponsored by the Company are currently ongoing in the following illnesses:

Malignant melanoma

Multiple myeloma

Chronic lymphocytic leukemia

Non-randomized Phase 2a or Phase 2b studies are currently being conducted in:

Acute myeloid leukemia

Chronic lymphocytic leukemia

Prostate cancer

The Company under its own Sponsorship, or under agreement with the National Cancer Institute, has recent or ongoing studies in:

Colon cancer

Small cell lung cancer

Acute leukemia

Breast cancer

The Company's clinical trials program is subject to change, and new initiatives in various diseases are under active review.

### Safety

Genasense™ has been administered to more than 250 patients worldwide since 1995. In general, the important side effects of Genasense™ are similar to the most important side effects of cancer chemotherapy; therefore, neither the dose nor the treatment schedule of accompanying therapy in the Phase 3 studies will be significantly altered.

### Further Information

Physicians who wish further information regarding the clinical trials programs, who wish to refer patients for consideration regarding entry into the clinical trials, or who wish to participate as sites should contact the Company by e-mail at: [ClinicalTrials@genta.com](mailto:ClinicalTrials@genta.com); or by telephone at: 908 255 1000. Clinical trial sites are subject to change during the course of clinical trials.

# GENTA INITIATES MULTICENTER TRIAL WITH GENASENSE™ IN AGGRESSIVE NON-HODGKIN'S LYMPHOMA

*Rituxan®-based Trial Moves to Front-line Lymphoma Treatment*

Berkeley Heights, NJ, February 19, 2002 – Genta Incorporated (NASDAQ: GNTA) announced today the initiation of a multicenter trial in patients with non-Hodgkin's lymphoma (NHL). The study will test Genta's lead antisense drug, Genasense™, in combination with Rituxan® (rituximab; Genentech Inc. and IDEC Inc.) plus standard chemotherapy in patients with a highly aggressive form of NHL, known as mantle cell lymphoma (MCL).

Clinical studies published in both *The Lancet* and the *Journal of Clinical Oncology* have reported preliminary safety and efficacy results of Genasense used alone as treatment for patients with advanced NHL. More recent preclinical data from several laboratories have shown high levels of synergy when Genasense was combined with both standard chemotherapy as well as Rituxan. The current trial will initially employ Genasense alone, followed by combined therapy with Genasense, Rituxan and a standard chemotherapy regimen (known as "CHOP").

MCL is a subset of NHL that is characterized by several molecular abnormalities, including over-expression of cyclinD1 and Bcl-2. Bcl-2 is a protein that blocks the onset of cancer cell death (known as apoptosis). NHL cells preferentially express high levels of this blocking factor, which may contribute to the failure of current types of anticancer therapy. Genasense lowers Bcl-2 and may therefore amplify the effectiveness of cancer treatment.

"Patients with mantle cell lymphoma still have a poor outcome with standard CHOP chemotherapy," commented Dr. Raymond P. Warrell, Jr., Chairman and CEO. "This new study builds on extensive prior experience with Genasense in various lymphoid diseases, such as NHL, myeloma and chronic lymphocytic leukemia. Rituxan has emerged as an important new therapy for NHL. The trial includes both newly diagnosed as well as relapsed patients, and it nicely complements our related development program with Ganite™ in this illness."

Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on anticancer therapy. The Company's research platform is anchored by oligonucleotide chemistry, particularly applications of antisense and decoy aptamer technology. Genasense™, the Company's lead compound, has received "Fast Track" and "Orphan Drug" designation from the Food and Drug Administration. Genasense™ is currently undergoing late-stage, Phase 3 clinical testing in several clinical indications. Genta's pipeline also comprises a portfolio of small molecules, including gallium-containing compounds and Androgenics compounds. Genta aims to become a direct marketer of its pharmaceutical products in North America. For more information about Genta, please visit our website at: [www.genta.com](http://www.genta.com).

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SOURCE: Genta Incorporated

# GENTA INITIATES FRONT-LINE MULTICENTER TRIALS WITH GENASENSE™ IN ACUTE LEUKEMIA AND SMALL CELL LUNG CANCER

*Trials in Newly Diagnosed Patients Complement Extend Existing 2<sup>nd</sup>-Line Programs*

Berkeley Heights, NJ, February 11, 2002 – Genta Incorporated (NASDAQ: GNTA) announced today the initiation of two new multicenter trials in previously untreated patients with acute myeloid leukemia (AML) and small cell lung cancer (SCLC). Both studies, which test Genta's lead antisense drug (Genasense™) in combination with standard chemotherapy, are intended as "lead-ins" to future randomized trials.

The AML trial will test Genasense in combination with daunorubicin and cytarabine in newly diagnosed patients older than 59 years of age. The study will initially start at Ohio State University, whose investigators had previously conducted a Phase I trial with Genasense in AML. The SCLC trial, which has been initiated at the University of Chicago, will evaluate Genasense in combination with carboplatin and etoposide in patients with extensive disease. The primary endpoints of both studies are to make a preliminary determination of safety and efficacy of the combinations. Both studies are being conducted pursuant to Genta's Cooperative Research and Development Agreement (CRADA) with the U.S. National Cancer Institute.

"These new trials expand our existing portfolio of clinical studies in lung cancer and AML, which to date have been conducted solely in relapsed patients, into newly diagnosed individuals," commented Dr. Raymond P. Warrell, Jr., Genta's Chairman and CEO. "The new AML study targets the same patient population as our current Phase 2 study of Genasense plus Mylotarg® (gemtuzomab ozogamicin). The SCLC trial complements our ongoing second-line trial of Genasense plus Taxotere® (docetaxel) in patients with non small cell lung cancer. In addition, these two studies further round out our development program by including combination drugs that have not previously been examined in clinical settings."

Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on anticancer therapy. The Company's research platform is anchored by oligonucleotide chemistry, particularly applications of antisense and decoy aptamer technology. Genasense™, the Company's lead compound, has received "Fast Track" and "Orphan Drug" designation from the Food and Drug Administration. Genasense™ is currently undergoing late-stage, Phase 3 clinical testing in several clinical indications. Genta's pipeline also comprises a portfolio of small molecules, including gallium-containing compounds for treatment of diseases associated with accelerated bone loss, and Androgenics compounds for prostate cancer. Genta aims to become a direct marketer of its pharmaceutical products in North America. For more information about Genta, please visit our website at: [www.genta.com](http://www.genta.com).

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SOURCE: Genta Incorporate

# Molecular Target of Genasense™ Therapy Reaffirmed at ASH Meeting

## - Results Support Ongoing Phase 3 Trial Design in Myeloma -

BERKELEY HEIGHTS, N.J., Dec. 10 /PRNewswire/ -- Genta Incorporated (Nasdaq: GNTA - news) today announced the presentation of new clinical and preclinical data supporting the activity of Genasense™ in two types of blood cancer, multiple myeloma and a related disorder known as Waldenstrom's macroglobulinemia. Genasense is the Company's lead antisense compound that is currently in several Phase 3 clinical trials. The results were presented over the weekend at the 43rd annual meeting of the American Society of Hematology (ASH) in Orlando, Florida.

Genasense shuts down production of a protein in cancer cells known as Bcl-2, which is believed to be a key factor in chemotherapy resistance. Prior studies have shown that Bcl-2 is over-expressed in many types of cancer, including most patients with multiple myeloma. In a new study presented by investigators from the University of Maryland, Bcl-2 was also found to be highly expressed in all patients with Waldenstrom's macroglobulinemia, a disease of malignant lymphoid cells that is similar to myeloma.

A second abstract was presented by investigators from the University of Texas -- San Antonio who had previously shown that Bcl-2 expression was a major cause of chemotherapy resistance in myeloma. Using cultured myeloma cells, Genasense was shown to down-regulate expression of the Bcl-2 protein. Moreover, such treatment was found to synergistically increase the killing of myeloma cells that was initiated by two chemotherapy drugs (dexamethasone and paclitaxel [Taxol®; Bristol Myers Squibb, Inc.]), as well as a form of gene therapy (adenovirus p53). The best responses in this study were observed using Genasense in combination with dexamethasone.

Lastly, in a separate presentation, a group from Nantes, France independently confirmed the effectiveness of the Bcl-2 antisense/dexamethasone combination in myeloma. This group also showed that antisense-mediated depletion of a related protein (Bcl-xL) was ineffective when it was used either alone or in combination.

"Collectively, this series of presentations confirms that Bcl-2 is a critical factor in myeloma and is a key target for antisense-directed therapy," said Dr. Stanley R. Frankel, Genta's Director of Clinical Operations. "At last year's ASH meeting, there was speculation that Bcl-xL might be a better target for an antisense attack in myeloma. However, data presented earlier this year at the AACR meeting showed that depletion of Bcl-xL actually increased resistance to chemotherapy. This new information that shows Bcl-xL targeting is ineffective in myeloma strongly argues for the primacy of Bcl-2 as a key anti-apoptotic factor. These data also confirm that the Genasense/dexamethasone combination that is currently being tested in our Phase 3 multicenter trial is one of the most promising new approaches to this disease."

Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on anticancer therapy. The research platform is anchored by oligonucleotide chemistry, particularly applications of antisense and decoy aptamer technology. Genasense™, the Company's lead compound, has received "Fast Track" and "Orphan Drug" designation from the Food and Drug Administration. Genasense™ is currently undergoing late-stage, Phase 3 clinical testing in several clinical indications. Genta's pipeline also comprises a portfolio of small molecules, including gallium-containing compounds for treatment of diseases associated with accelerated bone loss, and Androgenics compounds for prostate cancer. Genta aims to become a direct marketer of its pharmaceutical products in North America. For more information about Genta, please visit our website at: [www.genta.com](http://www.genta.com).

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# Investigators Report Results of Genasense™ Studies in Acute Leukemia

BERKELEY HEIGHTS, N.J., Dec. 10 /PRNewswire/ — Genta Incorporated (Nasdaq: **GNTA** - news) today announced the presentation of both clinical and preclinical data supporting the activity of Genasense™, the Company's lead antisense compound, in acute myeloid leukemia (AML).

The results were presented this weekend at the 43rd annual meeting of the American Society of Hematology (ASH) in Orlando, Florida. Final results of a dose-ranging study in patients with acute leukemia were published by a group from Ohio State University. Twenty patients, all of whom had relapsed from extensive prior treatment, received Genasense at daily doses of either 4 or 7 mg/kg/day for 10 days, plus combination chemotherapy with varying doses of two standard drugs, fludarabine and cytarabine. Three of six patients treated with the highest doses of all drugs achieved complete remission. The overall response rate for all patients at all dose levels was 45%, despite prior treatment with high-dose cytarabine in many patients.

A second presentation, from investigators at the University of Texas M. D. Anderson Cancer Center, tested Genasense alone and in combination with a monoclonal antibody (Mylotarg® [gemtuzumab ozogamicin; Wyeth Ayerst Laboratories, Inc.]) in AML cells. After 72 hours of treatment, Genasense decreased Bcl-2 protein (i.e. the target of Genasense activity) in leukemia cells by 50%. Genasense was then shown to amplify leukemic cell death that was induced by Mylotarg. These data are similar to recent results that show synergy with another monoclonal antibody, rituximab (Rituxan®; IDEC Pharmaceuticals), in two other preclinical studies.

"These abstracts are of interest for two reasons," noted Stanley R. Frankel, M.D., Genta's Director of Clinical Operations. "First, we will shortly be initiating a new multicenter clinical trial of Genasense used as front-line therapy in combination with two standard drugs (cytarabine and daunorubicin) in older patients with AML. Second, Genta is currently conducting a clinical trial of Genasense in combination with Mylotarg in this same patient population. Together, results showing synergy of Genasense in combination with each of these agents provide strong support for the use of these combinations."

Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on anticancer therapy. The research platform is anchored by oligonucleotide chemistry, particularly applications of antisense and decoy aptamer technology. Genasense™, the Company's lead compound, has received "Fast Track" and "Orphan Drug" designation from the Food and Drug Administration. Genasense™ is currently undergoing late-stage, Phase 3 clinical testing in several clinical indications. Genta's pipeline also comprises a portfolio of small molecules, including gallium-containing compounds for treatment of diseases associated with accelerated bone loss, and Androgenics compounds for prostate cancer. Genta aims to become a direct marketer of its pharmaceutical products in North America. For more information about Genta, please visit our website at: [www.genta.com](http://www.genta.com).

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SOURCE: Genta Incorporated

## **· GENTA AND NCI EXPAND JOINT CLINICAL TRIALS PROGRAM WITH GENASENSE™ TO INCLUDE NEW TYPES OF CANCER**

Berkeley Heights, NJ, November 14, 2001 –Genta Incorporated (Nasdaq: GNTA) today announced that the Company had expanded its relationship with the U.S. National Cancer Institute (NCI) for new clinical trials involving its lead antisense compound, Genasense™. Pursuant to an existing Cooperative Research and Development Agreement (CRADA), NCI has solicited new proposals from investigators to study Genasense™ in combination with standard anti-cancer therapy. Specific trials were requested in a broad group of diseases, including cancer of the prostate, breast, lung, colon, bladder, ovary, uterus, kidney and pancreas, and in Merkel cell tumor and non-Hodgkin's lymphoma. Under the CRADA terms, NCI and Genta will jointly review and approve the initiation of trials of highest clinical and scientific interest.

"Genta is delighted to expand its relationship with NCI into a number of diseases that have previously been tested only in the preclinical setting," said Dr. Loretta M. Itri, Genta's Executive Vice-President for Clinical Research and Chief Medical Officer. "This expanded collaboration will make Genasense™ readily available for new clinical trials in patients suffering from many types of cancers that are not currently part of the Company's clinical development program."

Genasense™ reduces levels of a protein called Bcl-2 in cancer cells by an "antisense" mechanism that knocks out the production of the protein. Research suggests that Bcl-2 is a major factor that contributes to chemotherapy resistance of cancer cells. The Company's programs are designed to test whether Genasense™, when used as pretreatment in patients who are receiving chemotherapy, can significantly enhance anticancer activity.

Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on anticancer therapy. The research platform is anchored by oligonucleotide chemistry, particularly applications of antisense and decoy aptamer technology. Genasense™, the Company's lead compound, has received "Fast Track" and "Orphan Drug" designation from the Food and Drug Administration. Genasense™ is currently undergoing late-stage, Phase 3 clinical testing in several clinical indications. Genta's pipeline also comprises a portfolio of small molecules, including gallium-containing compounds for treatment of diseases associated with accelerated bone loss, and Androgenics compounds for prostate cancer. Genta aims to become a direct marketer of its pharmaceutical products in North America. For more information about Genta, please visit our website at: [www.genta.com](http://www.genta.com).

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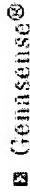
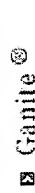
Committed  
to developing  
new possibilities  
in cancer care.



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## Innovation in Cancer Care

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### Randomized Trials

#### Phase 3 Trial in Chronic Lymphocytic Leukemia

This randomized trial investigates whether the addition of Genasense to standard treatment is superior to standard treatment alone. Standard treatment consists of cyclical treatment with a combination of two chemotherapy drugs, fludarabine and cyclophosphamide. The trial is limited to patients who have previously received and have relapsed from other therapies. *Trial Closed to Accrual*

#### Phase 3 Trial in Malignant Melanoma

This randomized trial investigates whether the addition of Genasense to standard treatment is superior to standard treatment alone. Standard treatment consists of a drug called dacarbazine (DTIC), which is administered once every 3 weeks. This trial is limited to patients with advanced-stage disease who have not previously received chemotherapy. (Prior vaccine or immunotherapy is allowed.) *Trial Closed to Accrual*

#### Phase 3 Trial in Multiple Myeloma

This randomized trial investigates whether the addition of Genasense to standard treatment is superior to standard treatment alone. Standard treatment consists of cyclical treatment with high-dose dexamethasone (a cortisone-like drug). The trial is limited to patients who have previously received and have relapsed from other therapies. *Trial Closed to Accrual*

The Company, under its own Sponsorship, or under its clinical research and development agreement (CRADA) with the National Cancer Institute, has ongoing non-randomized clinical trials in:

#### Non-Randomized

Small-cell Lung Cancer  
 Acute Myeloid Leukemia

#### Randomized

Non-small Cell Lung Cancer  
 Small-cell Lung Cancer

- Breast Cancer  
Liver Cancer  
Renal Cancer  
Non Hodgkin's Lymphoma  
Multiple Myeloma  
Colon Cancer  
Pancreatic Cancer  
Pediatric Solid Tumors  
Waldenstrom's
- Prostate Cancer

**Further Information**

All of the Company's clinical trials have additional restrictions and provisions for safety that may affect patient eligibility. Physicians who wish further information regarding the clinical trials programs, who wish to refer patients for consideration regarding entry into the trials, or who require information regarding current participating sites should contact the Company by e-mail at: [ClinicalTrials@genta.com](mailto:ClinicalTrials@genta.com); or by telephone at: 1-888-TOGENTA - (1-888-864-3682).

Participating sites are subject to change during the course of clinical trials.

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**Genasense® Phase 3 Results in Malignant Melanoma Updated at ASCO**

*Extended Follow-up Confirms Significant Increases in Complete Response, Durable Response, Progression-Free Survival, and Near-Significant Improvement in Overall Survival;*

Genta to File Marketing Authorization Application in Europe

**BERKELEY HEIGHTS, NJ – May 16, 2005 – Genta Incorporated (NASDAQ: GNTA)** announced long-term follow-up results from the Company's Phase 3 trial of Genasense (oblimersen sodium) Injection in patients with advanced malignant melanoma. Earlier analyses showed that the addition of Genasense to chemotherapy yielded a statistically significant increase in overall response, complete response, and time-to-progression. Extended follow-up for a minimum of 24 months in all patients has revealed that patients treated with Genasense also achieved a significant increase in "durable" response (i.e., responses longer than 6 months duration) (P=0.02) and a near-significant trend toward increased overall survival (P=0.077). Lastly, the analyses showed that a blood test (LDH) could be used to identify patients who were likely to derive maximal benefit from Genasense treatment. The results were presented by Dr. John Kirkwood, Director of the Melanoma Program and Professor of Medicine at the University of Pittsburgh, on Saturday at the annual meeting of the American Society of Clinical Oncology (ASCO) in Orlando, FL. A summary of efficacy end-points from the trial appears in the table below.

End-Point	Genasense/DTIC vs. DTIC	P
Overall response	12.4% vs. 6.8%	0.007
Complete response	3% vs. 0.5%	0.02

Durable response	7% vs. 3%	0.02
Progression-free survival, median	2.4 vs. 1.6 mos.	0.0003
Overall survival, median	9.0 vs. 7.8 mos.	0.077
Overall survival: LDH < or = 2 x normal, median	10.2 vs. 8.7 mos.	0.02

"This is the first randomized trial in metastatic melanoma that has ever shown significant superiority to dacarbazine across an array of clinical benefit end-points" noted Dr. Kirkwood. "These data suggest that the addition of Genasense to chemotherapy for metastatic melanoma offers the opportunity for durable benefits and prolonged survival in patients with this devastating disease."

"We are very gratified that meticulous follow-up conducted by the Genta clinical team has yielded such important results for patients with melanoma", said Dr. Raymond P. Warrell, Jr., Genta's Chairman and Chief Executive Officer. "We are pleased to announce that the Company intends to prepare a Marketing Authorization Application (MAA) for the European Medicines Agency (EMA), which will be based upon the extended follow-up in this trial. We have amended the current clinical protocol to enable 5 years of minimum follow-up on all patients, and we look forward to initiation of new clinical trials in patients with melanoma using Genasense combined with other active agents."

To facilitate the MAA filing, last year Genta formed a European-based subsidiary, Genta Development, Limited, that is based in London. Mr. William Keane, Genta's Senior Vice- President and Chief Financial Officer, was named Director of Genta Development, Limited, and Dr. Erard Gilles has been appointed General Manager. Dr. Gilles joins Genta after serving as Senior Director, Global Clinical Leader, Oncology Research and Development, at Johnson & Johnson PRD. Previously, he was Global Clinical Director, Oncology, at Aventis. He has also served in oncology research positions at Pharmacia and Roche in France. Prior to joining the pharmaceutical industry, Dr. Gilles was Assistant Professor in Oncology at the Institut Gustave Roussy, Villejuif, France.

In May 2004, a New Drug Application (NDA) based on 6-months of minimum follow-up data from this trial failed to receive an affirmative vote for approval by an advisory committee to the Food and Drug Administration. Genta subsequently withdrew that application, and the Company has not yet made a decision regarding re-filing the U.S. application.

**Study Design, End-points, and Enrollment**

Patients with Stage 4 metastatic melanoma or Stage 3 disease that was not surgically resectable were eligible for this trial. Patients were randomly assigned to receive dacarbazine (a standard chemotherapy drug) alone or in combination with Genasense. Prior to randomization, patients were stratified into 3 risk

categories: performance status (ECOG 0 vs. 1 or 2); presence or absence of liver metastases; and non- visceral disease and normal LDH vs. visceral disease or elevated LDH. (LDH is a blood test that is commonly used as a surrogate marker of disease activity, and high levels are strongly correlated with poor prognosis in advanced melanoma.) The primary endpoint of the trial was to compare overall survival between the two treatment arms using an intent-to-treat (ITT) analysis. Secondary endpoints included comparative analyses of tumor response (including complete response, overall response [complete plus partial response], and durable response), progression- free survival (PFS), and safety. A total of 771 patients were enrolled. Stratification achieved good balance across the various risk factors. The median age of patients who enrolled in the trial was 60 years.

#### **Overall Survival**

ITT analysis of all patients showed that the addition of Genasense to dacarbazine improved median survival to 9.0 months, compared with 7.8 months for patients treated with dacarbazine alone. The hazard ratio (HR) was 0.87. The difference represented a strong trend that approached but did not reach statistical significance ( $P=0.077$ ).

Due to the prospective specification of LDH as a component of stratification, the interaction of baseline LDH and treatment was also examined. Patients with normal LDH at baseline (defined as  $<$  or  $=$  1.1 times the upper limit of normal) had significant improvement in overall survival (hazard ratio  $=$  0.80;  $P=0.02$ ). Exploratory analyses were performed to examine the strength of this observation using increasing cutoffs of LDH. Patients with baseline LDH up to twice the upper limit of normal also showed a significant increase in survival (HR= 0.82;  $P= 0.02$ ).

#### **Overall, Complete, and Durable Responses**

Using conservative RECIST criteria, the overall response rate (complete plus partial responses) was 12.4% for patients treated with Genasense plus dacarbazine compared with 6.8% for patients treated with chemotherapy alone ( $P=0.007$ ). The complete response rates were 3% and 0.5%, respectively ( $P=0.02$ ). The number of patients who achieved durable responses exceeding 6 months in duration was 7% and 3%, respectively ( $P=0.02$ ). Due to limited follow-up, prior analysis had not revealed the difference in durable response.

Responses in this study were subjected to a new, independent, blinded review that demonstrated a high degree of concordance with earlier assessments that used investigator measurements and computer calculations of response according to RECIST criteria.

#### **Progression-Free Survival**

For the ITT population, patients treated with Genasense plus dacarbazine showed a significant increase in median progression-free survival to 2.4 months, compared with 1.6 months for patients treated with dacarbazine alone (HR=0.73;  $P=0.0003$ ). The robust nature of the PFS finding was confirmed by multiple sensitivity analyses.

**Safety**

The addition of Genasense to dacarbazine was not associated with serious, previously unreported adverse reactions compared with the use of dacarbazine alone. Adverse events that were significantly greater in the Genasense treatment group included but were not limited to nausea, vomiting, neutropenia, thrombocytopenia, fever, and catheter-related complications. The number of treatment-emergent adverse events associated with a fatal outcome on the study or within 30 days from last treatment was equal between the two treatment arms. Additional safety information from this trial can be accessed:

[http://www.fda.gov/ohrms/dockets/ac/04/briefing/4037B1\\_01\\_Genta-Genasense.htm](http://www.fda.gov/ohrms/dockets/ac/04/briefing/4037B1_01_Genta-Genasense.htm)

**About Genasense**

Genasense is the first oncology drug of its kind to directly target the biochemical pathway (known as apoptosis) whereby cancer cells are ultimately killed by chemotherapy. Genasense is believed to inhibit the production of Bcl-2, a protein that is highly expressed in malignant melanoma and is believed to be a fundamental cause of resistance to anticancer therapy. By inhibiting Bcl-2 Genasense may greatly improve the activity of anticancer therapy.

**About Melanoma**

Malignant melanoma is the most deadly form of skin cancer. The incidence of this disease is increasing by approximately 4% annually in the US. In the year 2000, almost 50,000 cases of malignant melanoma were diagnosed. Melanoma is the number one cause of cancer death in women aged 25 to 30. For more information on melanoma please visit :

[http://www.nci.nih.gov/cancer\\_information/cancer\\_type/melanoma](http://www.nci.nih.gov/cancer_information/cancer_type/melanoma)

**About Genta**

Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on delivering innovative products for the treatment of patients with cancer. The Company's research platform is anchored by two major programs that center on oligonucleotides (RNA and DNA-based medicines) and small molecules. Genasense® (oblimersen sodium) Injection, the Company's lead compound from its oligonucleotide program is currently undergoing late-stage, Phase 3 clinical testing. The leading drug in Genta's small molecule program is Ganite® (gallium nitrate injection), which the Company is exclusively marketing in the U.S. for treatment of patients with cancer-related hypercalcemia that is resistant to hydration. For more information about Genta, please visit our website at: [www.genta.com](http://www.genta.com).

*This press release contains forward-looking statements with respect to business conducted by Genta Incorporated. By their nature, forward-looking statements and forecasts involve risks and uncertainties because they relate to events and depend on circumstances that will occur in the future. There are a number of factors that could cause actual results and developments to differ materially. For a discussion of those risks and uncertainties, please see the Company's Annual*



*Report/Form 10-K for 2004.*

SOURCE: Genta Incorporated

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**Innovation in Cancer Care**

**Updated Analysis from Phase 3 Trial of Genasense® in CLL Shows Significant Increase in Duration of Major Responses**

**BERKELEY HEIGHTS, NJ – May 13, 2005** – Genta Incorporated (NASDAQ: GNTA) today announced an update of results from the Company's Phase 3 trial of Genasense (oblimersen sodium) Injection in patients with relapsed or refractory chronic lymphocytic leukemia (CLL). Preliminary results of this trial announced in December 2004 showed that the trial had achieved its primary end-point, which was to demonstrate a statistically significant increase in the proportion of patients who achieved either a complete response (CR) or a nodular partial response (nPR). With an additional 6 months of follow-up, one additional patient in the Genasense treatment group has achieved a nPR. Overall, 20 patients (17%) in the Genasense plus chemotherapy group achieved a CR or nPR compared with 8 patients (7%) in the chemotherapy only group ( $P=0.025$ ). Moreover, extended follow-up has now shown that the duration of CR/nPR is significantly superior for patients in the Genasense treatment group ( $P=0.035$ ). Five of 8 patients (63%) have relapsed on the chemotherapy only arm compared with 4 of 20 patients (20%) on the Genasense treatment arm.

"For the first time, these updated results enable a direct comparison of the quality of major responses that were achieved in the Phase 3 Genasense trial", said Dr. Raymond P. Warrell, Jr., Genta's Chairman and Chief Executive Officer. "Having achieved the primary end-point, the additional follow-up has shown not only that most major responses on the Genasense arm are durable (that is exceeding 6 months in duration), but also that their duration is significantly superior to those achieved using chemotherapy alone."

**Study Design, Patient Enrollment and Adverse Experience**

Patients were eligible for this trial if they had failed standard treatment for CLL that had included fludarabine. Two hundred forty one patients were randomized to receive standard chemotherapy with fludarabine and cyclophosphamide with or without Genasense. In the trial, 120 patients were randomized to receive Genasense plus chemotherapy, and 121 patients were randomized to receive chemotherapy alone. During the study, the incidence of any Grade 3 or Grade 4 serious adverse event was higher in the Genasense group. Specific events that

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were significantly higher in the Genasense group included (but were not limited to) thrombocytopenia, nausea, fever, fatigue, back pain, weight loss, dehydration, and intravenous catheter complications. However, serious adverse events that resulted in discontinuation of therapy were equal between the treatment arms. Treatment-emergent adverse events that led to deaths on study or within 30 days from last treatment occurred in 9 patients in the Genasense group and 5 patients in the chemotherapy alone group. Other efficacy and safety information from the trial can be accessed at:

[http://www.genta.com/Genta/InvestorRelation/2004/press\\_20041206.html](http://www.genta.com/Genta/InvestorRelation/2004/press_20041206.html)

#### **About Chronic Lymphocytic Leukemia**

CLL is the most common form of leukemia in adults. According to the American Cancer Society, approximately 8,000 patients will be diagnosed this year, and more than 60,000 people are living with CLL in the United States. The disease arises in lymphocytes, a type of white blood cell that normally produces antibodies and serves important immune functions. Patients with CLL typically develop symptoms that may progress over a period of years, ultimately producing a generalized depression of immunity, marked increases in the size of spleen, liver and lymph nodes, and impaired production of other normal blood cells. Eventually, these problems may cause life-threatening complications, such as overwhelming infections and fatal bleeding. For more information about CLL, visit <http://www.leukemia-lymphoma.org>.

#### **About Genasense**

Genasense inhibits production of Bcl-2, a protein made by cancer cells that is thought to block chemotherapy-induced apoptosis (programmed cell death). By reducing the amount of Bcl-2 in cancer cells, Genasense may enhance the effectiveness of current treatments for CLL. Genta is pursuing a broad clinical development program with Genasense evaluating its potential to treat various forms of cancer.

#### **About Genta**

Genta Incorporated is a biopharmaceutical company with a diversified product portfolio that is focused on delivering innovative products for the treatment of patients with cancer. The Company's research platform is anchored by two major programs that center on oligonucleotides (RNA and DNA-based medicines) and small molecules. Genasense® (oblimersen sodium) Injection, the Company's lead compound from its oligonucleotide program is currently undergoing late-stage, Phase 3 clinical testing. The leading drug in Genta's small molecule program is Ganite® (gallium nitrate injection), which the Company is exclusively marketing in the U.S. for treatment of patients with cancer-related hypercalcemia that is resistant to hydration. For more information about Genta, please visit our website at: [www.genta.com](http://www.genta.com).

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